REMARKS

I. Status of the Claims

Claims 1-124 were originally filed and are cancelled herein in favor of new claims 125-154. Upon entry of the present amendment, all the claims will be directed to cell-based assays that use a particular human receptor to identify compounds having a known effect on olfactory perception that modulate the activity of a particular human olfactory receptor and methods of identifying compounds that putatively modulate (enhance or inhibit) or mimic the effect of said compound based on whether they modulate or mimic the effect of said known olfactory compound on the activity of said olfactory receptor polypeptide in said cell-based assay the effect of said compound in said cell-based assay. Specific support for the assay claims may be found at least in the disclosure at pages 71-81 of the application, most especially at pages 71-75.

II. Response to Outstanding Objectives Regarding the Figures

A revised sequence listing is being prepared which will include references to the sequences in the figures.

III. Response to Prior Outstanding Rejections

Because of the shift in Applicant's election (coupled with the filing an RCE request herein), Applicants only address the rejections that potentially may be applicable to the new assay claims.

Particularly, Applicants note that the prior elected claims were rejected under 35 U.S.C. § 101 and § 112 enablement and written description grounds on the basis that Applicants allegedly did not identify a well established utility for hAOLFR29 or enable or establish possession of the invention as it pertained to the elected OR DNA sequence. The criticism was that the as-filed disclosure did not enumerate any ligands that specifically bind to the elected receptor polypeptide.

In support of the rejection, the Examiner quotes from a recently issued Johns Hopkins patent (Specifically, he refers to the exclusively licensed by the assignee of this application), US Patent 6,492,143 the following text:

> "to analyze odorant ligand-receptor interactions and their effects on cell physiology, it is first necessary to identify specific odorant/ligand(s) and the olfactory receptor to which they specifically bind."

The Examiner suggests that this supports a conclusion that the claims lack utility and are not enabled or sufficiently described by the technology of the as-filed application. Applicants respectfully traverse this rejection, to the extent that it may be applicable to the current assay claims.

With respect thereto, Applicants respectfully submit that the as-filed application contains sufficient information to establish a credible utility and further satisfies the enablement and written description requirements. In particular, the specification correctly identifies that the elected DNA sequence is a GPCR (based on its characteristic 7-transmembrane domain structure) and further correctly identifies that this DNA encodes an olfactory receptor based (1) on the fact that this

receptor polypeptide is expressed in olfactory neurons and further (2) based on its level of sequence identity to other human olfactory receptor gene sequences as well as the presence of conserved sequence motifs that are contained in numerous (hundreds of) other human olfactory receptors comprised in this same olfactory receptor gene family. (See page 24 of the subject application). Also, these identified sequences contain very close matches to those seen in other species olfactory receptor sequences (See Mombaerts *Ann. Rev.* 22:487-50 (1999) and *Pilpel et al Protein Science* 8:967-77 (1999)).

Contrary to the Office Action, Applicants respectfully submit that this information would be regarded to be sufficient to reasonably establish to one skilled in the art that nucleic acid sequence having SEQ ID NO: 56 indeed encodes an olfactory receptor.

Moreover, while not contained in the as-filed disclosure, Applicants further respectfully submit that later reported bioinformatics, genetic and sensory analysis data supports a conclusion that the DNA contained in SEQ ID NO: 56 is involved in detecting the smell of androsterone, a component of sweat and that alleles of this gene correlate to an inability to detect the smell of androsterone.

Applicants respectfully submit that this information is not necessary to enable, describe or establish the utility of the prior elected OR DNA sequence. However, it is relevant in that it substantiates that the disclosed hypothetical utility of the prior elected DNA sequence (that it encodes a GPCR involved in

olfaction) is valid. The facts herein are distinguishable from the classic orphan receptor based rejection wherein a receptor is claimed wherein the inventors are unclear of as to the function of the disclosed putative receptor. Herein, the inventors disclosed in the as-filed application, and later evidence substantiates this disclosure, that the subject DNA sequence encodes a receptor polypeptide that is involved in olfaction.

With respect to the assertion that it is necessary to identify a ligand bound by the elected DNA to establish a "demonstrable utility" this is vigorously disputed. To the contrary, as recited in the subject claims, the subject DNA, when expressed in cell-based systems may be used to specifically identify known olfactants that interact with this receptor. As described in the application, these assays will permit the detection of compounds that putatively mimic, enhance or block the odor elicited by the known olfactant. Thereby, the subject DNA ((as recited in the new claims) will permit the identification of compounds having potential application as deodorants, perfumes, fragrances and the like.

The efficacy and utility of such assays does not reside in the identification of a particular ligand. Indeed, one skilled in the art will be able to practice the claimed assay methods without any requisite knowledge of a ligand that specifically binds the elected OR receptor simply by screening libraries of known olfactants or by screening random compound libraries to identify those of which modulate the activity of this particular OR receptor.

In fact, a very significant application of the prior elected DNA sequence is as a screening agent that will facilitate a greater understanding of the complex biology of smell, and which will facilitate an identification of specific odorants that interact with this specific olfactory receptor. This understanding and the underlying assays claimed herein will further facilitate in the discovery of compounds that modulate the effect of known olfactorants on the activity of this particular human olfactory receptor.

Turning now to the remaining rejections raised against the prior elected claims, Applicants note that the claims were rejected on prior art grounds, specifically on the basis that the claims were anticipated or rendered obvious by Birren et al (Genbank Accession Number AC006313, January 26, 1999) or Burford et al (WO 2001/42288).

These rejections are not applicable against the current claims since neither of these references teaches or suggests that the polypeptide encoded by SEQ ID No: 56 would be useful in the assays recited in new claims 125-154 to identify compounds that putatively modulate (enhance, block or mimic) olfaction. Rather, at best, the references merely would suggest that the DNA sequence disclosed therein, based on its characteristic 7-transmembrane structure, encodes a GPCR, and provide no teaching otherwise as to its underlying function.

Therefore, the subject claims are believed to be free of the prior rejections and objections.

Based on the foregoing, entry of the newly submitted claims in favor of the prior elected claims is respectfully requested.

If there are any questions regarding this Preliminary Amendment or this application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and shortages in other fees, be charged, or any overpayment in fees be credited, to the Account of Crowell & Moring, LLP, P.L.L.C., Deposit Account No. 05-1323 (Docket #100337.54287).

Respectfully submitted,

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